## INTERNATIONAL SEARCH REPORT

International application No. PCT/AU2003/001356

## CLASSIFICATION OF SUBJECT MATTER Int. Cl. 7: C12N 15/12 C12N 15/63 C12N 5/16 A61K 48/00 A61K 38/45 According to International Patent Classification (IPC) or to both national classification and IPC В. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched SEE ELECTRONIC DATABASES Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) CAPLUS, WPIDS, MEDLINE, AGRICOLA, BIOSIS (sphingosine kinase, EC 2.7.1.91, overexpressi?, expressi?, endotheli?, huvec C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Category\* Relevant to claim No. US 2002042358 A (SPIEGEL) 11 April 2002. X See whole document. 1-43 WO 2002028906 A (BAYER AKTIENGESELLSCHAFT) 11 April 2002 X See whole document 1-43 WO 2002000887 A (MEDVET SCIENCE PTY. LTD.) 3 January 2002 See whole document X 1-43 X Further documents are listed in the continuation of Box C. $|\mathbf{x}|$ See patent family annex Special categories of cited documents: "A" document defining the general state of the art יידיי later document published after the international filing date or priority date which is not considered to be of particular and not in conflict with the application but cited to understand the principle or theory underlying the invention "E" earlier application or patent but published on or document of particular relevance; the claimed invention cannot be after the international filing date considered novel or cannot be considered to involve an inventive step when the document is taken alone document which may throw doubts on priority document of particular relevance; the claimed invention cannot be claim(s) or which is cited to establish the considered to involve an inventive step when the document is combined publication date of another citation or other special with one or more other such documents, such combination being obvious to reason (as specified) a person skilled in the art document referring to an oral disclosure, use, document member of the same patent family exhibition or other means document published prior to the international filing date but later than the priority date claimed Date of the actual completion of the international search Date of mailing of the international search report 15 JAN 2004 7 January 2004 Name and mailing address of the ISA/AU Authorized officer **AUSTRALIAN PATENT OFFICE** PO BOX 200, WODEN ACT 2606, AUSTRALIA DAVID OLDE E-mail address: pct@ipaustralia.gov.au

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C (Continua		7001330			
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.			
х	WO 2001085953 A (MEDVET SCIENCE PTY. LTD.) 15 November 2001 See whole document				
x	WO 2001074837 A (SANKYO COMPANY LIMITED et al) 11 October 2001 See whole document				
	WO 2000070028 A (JOHNSON & JOHNSON RESEARCH PTY. LIMITED) 23 November 2000.				
X	See whole document				
x	WO 1999012533 A (MEDVET SCIENCE PTY. LTD.) 18 March 1999 See whole document	1-43			
	WO 1999061581 A (OFFICE OF THE DEAN OF RESEARCH AND GRADUATE EDUCATION) 2 December 1999				
X	See whole document	1-43			
<b>X</b>	Katsuma, S. et al. 2002. Signalling mechanisms in sphingosine 1-phosphate-promoted mesangial cell proliferation. Genes to Cells. 7:1217-1230. See whole document.	1, 2, 4-26			
x	Nava, V.E. et al. 2002. Sphingosine kinase type 1 promotes estrogen-dependent tumorigenesis of breast cancer MCF-7 cells. Experimental Cell Research. 281:115-127. See whole document	1, 2, 4-26			
x	Ancellin, N. et al. 2002. Extracellular export of sphingosine kinase-1 enzyme. Sphingosine 1-phosphate generation and the induction of angiogenic vascular maturation. The Journal of Biological Chemistry. 277(8):6667-6675. See whole document	1, 2, 4-26			
P/X	Shu, X. et al. 2002. Sphingosine kinase mediates vascular endothelial growth factor-induced activation of Ras and mitogen-activated protein kinases. Molecular and Cellular Biology. 22(22):7758-7768.  See whole document	1-43			
	Vann, L.R. et al. 2002. Involvement of sphingosine kinase in TNF-α-stimulated tetrahydrobiopterin biosynthesis in C6 glioma cells. The Journal of Biological Chemistry. 277(15):12649-12656.				
Α	See whole document	1-43			
A	Spiegel, S. et al. 2002. Sphingosine 1-phosphate, a key cell signalling molecule. The Journal of Biological Chemistry. 277(29):25851-25854. See whole document	1-43			
A	Alemany, R. et al. 2001. Depolarisation induces rapid and transient formation of intracellular sphingosine-1-phosphate. FEBS Letters. 509:239-244.  See whole document	1.42			
A	See whole document	1-43			

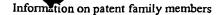


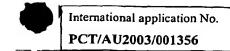


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Box I Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)							
This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:							
1. Claims Nos:							
because they relate to subject matter not required to be searched by this Authority, namely:							
2. X Claims Nos: 20-24, 27, 28, 43 partially							
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:							
These claims are directed to any agent, analogue, equivalent, mimetic, agonist or antagonist capable of modulating the functional level of SK. The scope of these terms is such that any and all known and unknown molecules or compounds are encompassed. This is clearly beyond the teaching and scope of the specification. Hence the search has been limited to the over-expression of sphingosine kinase and not to any and all molecules or compounds that may have this effect.							
3. Claims Nos:							
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)							
Box II Observations where unity of invention is lacking (Continuation of item 3 of first sheet)							
This International Searching Authority found multiple inventions in this international application, as follows:							
As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims							
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.							
As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:							
·							
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:							
Remark on Protest							
No protest accompanied the payment of additional search fees.							

## INTERNATIONAL SEARCH REPORT





This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member						
wo	1999061581	AU	40979/99	CA	2329124	EP	1235913	
wo	1999012533	AU	89658/98	CA	2302838	EP	1011654	
		US	2002051777					
wo	2002028906	AU	23593/02	EP	1326986	US	2003125533	
wo	2000070028	AU	45239/00	CA	2372541	EP	1192247	
wo	2001074837	AU	51002/01	CA	2404965	. CZ	20023282	
		EP	1268509	HU	0301691	NO	20024727	
		US	2002042101					
wo	2001085953	AU	56001/01	BR	0110759	CA	2408196	
		EP	1290182	NO	20025375			
wo	2002000887	AU	65699/01	CA	2414210	EP	1299548	
		NO	20026265				••	
US	2002042358		NONE					
				•			END OF ANNEX	